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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,633	06/08/2001	Preeti G. Lal	PC-0040 CIP	9282

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,633	LAL ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,28-31 and 33-42* is/are pending in the application.

4a) Of the above claim(s) *35-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,28-31,33,34 and 40-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/3/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 3, 2004 has been entered.

The amendment filed September 3, 2004 amending the specification to delete the line at page 9 reciting the percent identity to a clone not a sequence and amending claim 34 has been entered.

Claims 26, 28-31 and 33-42 are pending. Claims 35-39 are withdrawn.

Claims 26, 28-31, 33, 34 and 40-42 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 34 has been amended to be drawn to "An isolated polynucleotide having about 90% identity to a sequence of SEQ ID NO:2 from nucleotide 667 to nucleotide 1173". The Examiner is unable to locate adequate support in the specification for such limitation.

Applicants indicate support for the amended claim "at page 9, line 27 to page 10, line 2 (paragraph [**0052**] of U.S. 2002/0102569)" (Remarks, page 7). The Examiner is unable to locate adequate support for then amendment in the indicated texts. The specification at page 9, line 27 to page 10, line 2 as amended on February 12, 2004 concerns with identifying mammalian variants of human sequence of SEQ ID NO:2 using BLAST2. The mouse sequence (SEQ ID NO:10) is indicated as having 90% identity when nucleotides 667-1173 are aligned. Therefore, even if the alignment is correct, the specification at most provides support for the specific fragment of the mouse sequence. There is no support for any mammalian sequences or nucleotide sequences of any other origin or man made that have 90% identity to nucleotides 667-1173 of SEQID NO:2 other than mouse SEQ ID NO:10, if the alignment is correct. Furthermore, there is no support for "about 90%" as opposed to "90%" indicated in the specification. Thus there is no indication that a polynucleotide having about 90% identity to a sequence of SEQ ID NO:2 from nucleotide 667 to nucleotide 1173 was within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26, 28-31, 33, 34 and 40-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 26, 28-31, 33, 34 and 40-42 are directed to or depend from a DNA encoding SEQ ID NO:1. Applicants disclose a human nucleic acid sequence of SEQ ID NO: 2 encoding the protein having the amino acid sequence of SEQ ID NO:1. The asserted utility for SEQ ID NO:2 is as diagnostic of cancers, particularly lymphoma and cancer of the bladder, colon, kidney, ovary, and testis (page 3, lines 4-5). The specification teaches that SEQ ID NO:1 has 55% identity to both high-glucose-regulated protein 8 and NY-REN-2 antigen (page 8, lines 32-33). There is no additional data to support any function for the protein of SEQ ID NO:1. Neither high-glucose-regulated protein 8 nor NY-REN-2 antigen are used as diagnostic of cancer. The specification discloses the expression of SEQ ID NO:2 in various libraries, each library constructed from the tissue removed from a single individual. With regard to lymphoma (one library), expression was two-fold greater than in activated lymphocytes and six-fold greater than

in untreated or non-activated T-cells (page 32). The specification teaches that "no expression was seen in activated in three other libraries made from activated T-cells" (page 32, line 31). With regard to cancer of the colon, the specification teaches that in metastatic cancer (one library) the expression was higher than in contained tumor (one library) and two-fold greater than in normal tissue (page 32, line 33, through page 33, line 18). With regard to cancer of the bladder, the expression is higher in one library in transitional cell carcinoma of the bladder (BADTUT08) than in normal tissue (page 33). With regard to cancer of the kidney, the expression is higher in one library in Wilms' tumor, slightly higher in one library in renal cell carcinoma and less high in two other libraries in renal cell carcinoma compared with one library from normal cortex (page 34). With regard to the ovary, only in one metastatic endometrial cancer library and not in other cancerous and non-cancerous ovarian libraries the expression was greater (page 34). With regard to the testis, one library from testis tumor has higher expression than one library from embryonal carcinoma, the latter one higher than in normal tissue. Thus, it appears, that the specification presents data mostly obtained from one individual (one library) and compares it to library/libraries from other individuals. Unless the data are statistically significant, it is impossible to know whether the expression is indeed diagnostic of any cancer. It is known in the art that the expression of a protein can vary from one individual to another. On the other hand, in the state of cancer, the expression of most proteins is aberrant. Therefore, the specification provides no guidance as to how to correlate the expression of SEQ ID NO:2 and the specific cancer. Said correlation is not established in the prior art.

While the expression of SEQ ID NO:2 may be indicative of cancer, it may be due to other conditions as well. The expression of a gene can be affected by various conditions not necessarily associated with or occurring in any type of cancer. Overall, SEQ ID NO:2 appears to be expressed or not expressed in cancerous as well as non-cancerous tissues (*supra*, and page 34, lines 38-40, for example).

Thus, there is no showing in the specification that the expression of SEQ ID NO:2 is specifically occurring in lymphoma and cancer of the bladder, colon, kidney, ovary, and testis and not in other diseases or in healthy condition. Alternatively, there is no showing that the expression of SEQ ID NO:2 parallels the expression of any gene used as a direct diagnostic tool for any type of cancer.

However, in order for a polynucleotide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in tissue that is derived from cancer cells of one individual is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule in a statistically significant manner. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of

normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself.

Thus, obtaining of theoretically desired result of diagnosing lymphoma and cancer of the bladder, colon, kidney, ovary, and testis by measuring the expression of SEQ ID NO:2 is unpredictable based on the instant disclosure. A method for diagnosing of lymphoma and cancer of the bladder, colon, kidney, ovary, and testis would require or constitute carrying out further research to identify or reasonably confirm that cancer can be diagnosed using a DNA encoding SEQ ID NO:1.

Claim Rejections - 35 USC § 112

Claims 26, 28-31, 33, 34 and 40-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, with regard to claim 34, even if the utility for SEQ ID NO:2 and its 667-1173 fragment were established, a sequence that 90% identical thereto would not

necessarily have the same function/utility. Without knowing the function of a variant sequence that is 90% identical to the 667-1173 fragment of SEQ ID NO:2, it would require undue experimentation for one of ordinary skill in the art to use said variant sequence.

Response to Arguments

Applicant's arguments, see Remarks, pages 7-8, filed September 3, 2004, with respect to the 112, 1st paragraph, new matter rejection have been fully considered and are persuasive. The new matter rejection of claims 40-42 has been withdrawn.

The 102(a) rejection of claim 34 is withdrawn in view of the amendment.

Applicant's arguments filed September 3, 2004 with regard to the 101/112 rejection have been fully considered but they are not persuasive.

Applicants recite MPEP to argue that the claimed invention satisfies the requirements of 35 USC § 101. They argue that "***If an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on a lack of utility is n0t appropriate***" (page 10, emphasis in original). They continue "a *prima facie* showing must establish that it is ***more likely than not*** that a person of ordinary skill in the art would not consider that ***any utility asserted by the applicants*** would be specific and substantial" (*ibid*, emphasis in original). This is not persuasive because it unclear which result obtained with SEQ ID NO:2 that only partially successful is shown and discussed. Furthermore, Applicants apparently imply

that the possibility that SEQ ID NO:2 may be a potential marker for some cancer should result in the believe that it is more likely than not. It is further unclear which specific utilities are encompassed by "***any utility asserted by the applicants".*** Applicants assert that "*A. Transcripts encoding the cancer marker protein are differentially expressed in lymphoma*". ... "*B. Transcripts encoding the cancer marker protein are differentially expressed in metastatic adenocarcinoma of the colon*". ... "*C. Transcripts encoding the cancer marker protein were differentially expressed in transitional cell carcinoma of the bladder*". ... "*D. Transcripts encoding the cancer marker protein were differentially expressed in metastatic endometrial cancer*". ... "*E. Transcripts encoding the cancer marker protein were differentially expressed in testis tumor*" (pages 12-13). Applicants refer to the data presented on pages 32-35 of the specification. These arguments are not persuasive because no utility for SEQ ID NO:2 as a marker for metastatic endometrial cancer was asserted. As discussed above, the specification mentions lymphoma and cancer of the bladder, colon, kidney, ovary, and testis (page 3, lines 4-5). Applicants do not discuss the data related to cancer of kidney or ovary. However, with regard to cancer of the kidney, the specification teaches that the expression is higher in one library in Wilms' tumor, slightly higher in one library in renal cell carcinoma and less high in two other libraries in renal cell carcinoma compared with one library from normal cortex. It appears that these results suggest that SEQ ID NO:2 is not a marker for the kidney cancer. With regard to the ovary, only in one metastatic endometrial cancer library and not in other cancerous and non-cancerous ovarian libraries the expression was greater (pages 34-35). With regard to cancer of a specific

organ, there are known different types and stages of cancer. The specification did not assert for which type and stage of cancer, SEQ ID NO; 2 may serve as a marker. Most importantly, the results with the expression of SEQID NO:2 that are discussed by Applicants were obtained with a single cancer library that was compared with some other libraries from randomly selected tissues from other individuals that happen to be available for the experiment. It is known in the art that the expression of a protein can vary from one individual to another. On the other hand, in the state of cancer, the expression of most proteins is aberrant. Unless the data are statistically significant, which they are not, it is impossible to know whether the expression is indeed diagnostic of any cancer. Therefore, the specification provides no guidance as to how to correlate the expression of SEQ ID NO:2 and the specific cancer. Said correlation is not established in the prior art.

Applicants further argue that "*F. The protein designated by SEQ ID NO:1 may function as a cancer marker protein for cancer resulting from dermatomyositis*. In addition, the protein designated by SEQ ID NO:1 from amino acids 74-315 is 100% identical to a protein designated "Dermatomyositis ***associated with cancer*** putative autoantigen from amino acids 302-543" (pages 13-14). It is not agreed with that the data related to dermatomyositis can be relied on to supplement the instant specification, in order to meet the utility requirement of 35 USC§ 101 because the specification does not disclose or even mention the term "dermatomyositis" or its correlation with the expression of SEQ ID NO:2 or its fragment encoding residues 74-315 of SEQ ID NO:1. In conclusion Applicants argue that "based on the totality of the record, it is more likely

than not that a person of ordinary skill in the art would consider that ***at least one of the utilities asserted by the Applicants*** is specific, substantial, and credible" (page 16, emphasis in original). This is not agreed with because, as discussed above, Applicants did not assert the specific utilities for SEQ ID NO:2. The specification only provides some random data on the expression of SEQ ID NO:2. Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known specific disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Thus, the specification provides no basis for concluding that SEQ ID NO:2 is associated with any specific disease (cancer). Further research would be need to identify or reasonably confirm that any cancer can be diagnosed using a DNA of SEQ ID NO:2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

November 10, 2004